DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
5100 Paint Branch Parkway
College Park, Maryland 20740

MAR 5 2004

Edgar Drake, Ph.D.
President
Rocky Mountain Selenium, Inc.
2101 Ridge Road
Estes Park, Colorado 80517

Dear Dr. Drake:

This is to inform you that the notification, dated December 9, 2003, you submitted pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on December 23, 2003. Your notification concerns the substance "methylseleninic acid" that you intend to market as a new dietary ingredient.

The notification informs FDA that Rocky Mountain Selenium, Inc. intends to market the new dietary ingredient, "methylseleninic acid", in liquid form. The proposed dietary supplement will be used at a dose of 4 drops; each drop is specified as containing 50 µg of selenium in the form of "methylseleninic acid". The notification states that the label will contain the following instructions for use: "This product is for adults only. Take four drops daily as a dietary supplement. Do not exceed recommended dosage."

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under section 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has carefully considered the information in your submission, and the agency has concerns about the evidence on which you rely to support your conclusion that a dietary supplement containing "methylseleninic acid" will reasonably be expected to be safe.

No safety information or data specific to the product, methylseleninic acid, is provided. Two articles addressed the use of "methylseleninic acid" in mechanistic studies of selenium metabolism. The purpose of these studies was not directed at determining the safety of intake of methylseleninic acid in human populations. In addition, the notification does not provide any information regarding the history of use of "methylseleninic acid".

The notification contained thirteen references of pre-clinical and clinical studies conducted with selenium compounds. Three references were review articles on various forms of selenium. None specifically discussed methylseleninic acid. In many studies, baker's yeast was the source of selenium used. It is unclear how baker's yeast would compare to "methylseleninic acid" other than the comparison of selenium yield. Five references summarized numerous *in vitro* studies using a variety of selenium compounds in mouse mammary and leukemic cells. These articles mostly addressed the purported beneficial, i.e. anti-cancer, effects of selenium, rather than the evidence of safety.

One reference addressed the metabolism of selenium-containing compounds. "Methylseleninic acid" was discussed specifically. It inhibits cell growth and DNA synthesis at very low levels *in vitro*. It also has antiangiogenic effects. It appears to be a less toxic form of selenium in that it is metabolized beyond the hydrogen selenide pool. The author(s) state that because of this, it has no toxicity associated with it. Hydrogen selenide is a product of the metabolism of many selenium-containing compounds and has significant toxicity associated with its build-up. Two references discussed a mouse and a rat study using a variety of selenium-containing compounds, not including "methylseleninic acid". A final reference discussed a clinical trial in which patient's were given brewer's yeast which supplied 200 micrograms of selenium daily for an average of 4.5 years. No toxicity was observed.

Due to the minimal safety information submitted on methylseleninic acid, and the lack of information bridging the safety of this substance to the general selenium information submitted, it is unclear that there is reasonable assurance of safety for methylseleninic acid.

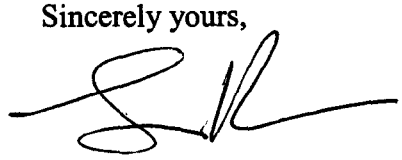
For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that "methylseleninic acid", when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. Therefore, your product may be adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury. Introduction of such a product into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

If you decide to submit a new notification, please describe your basis for determining that the substance you identify as the new dietary ingredient is included in the definition of a dietary ingredient under 21 U.S.C. 321(ff)(1).

Your notification will be kept confidential for 90 days after the filing date of December 23, 2003. After the 90-day date, the notification will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. Prior to that date, you may wish to identify in writing specifically what information you believe is proprietary, trade secret or otherwise confidential for FDA's consideration.

If you have any questions concerning this matter, please contact Victoria Lutwak at (301) 436-2375.

Sincerely yours,



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